



James Graham Brown Cancer Center

Molecular Targets
Center of Biomedical Research Excellence

Molecular Targets

Center for Biologic Research Excellence

- NIH Grant of \$12 M initially funded in 2003, refunded for \$11.5 M in 2008
- Has allowed recruitment of 11 young molecular biologists
- Will continue to stimulate programmatic growth with Wendell Cherry and Kosair Programs

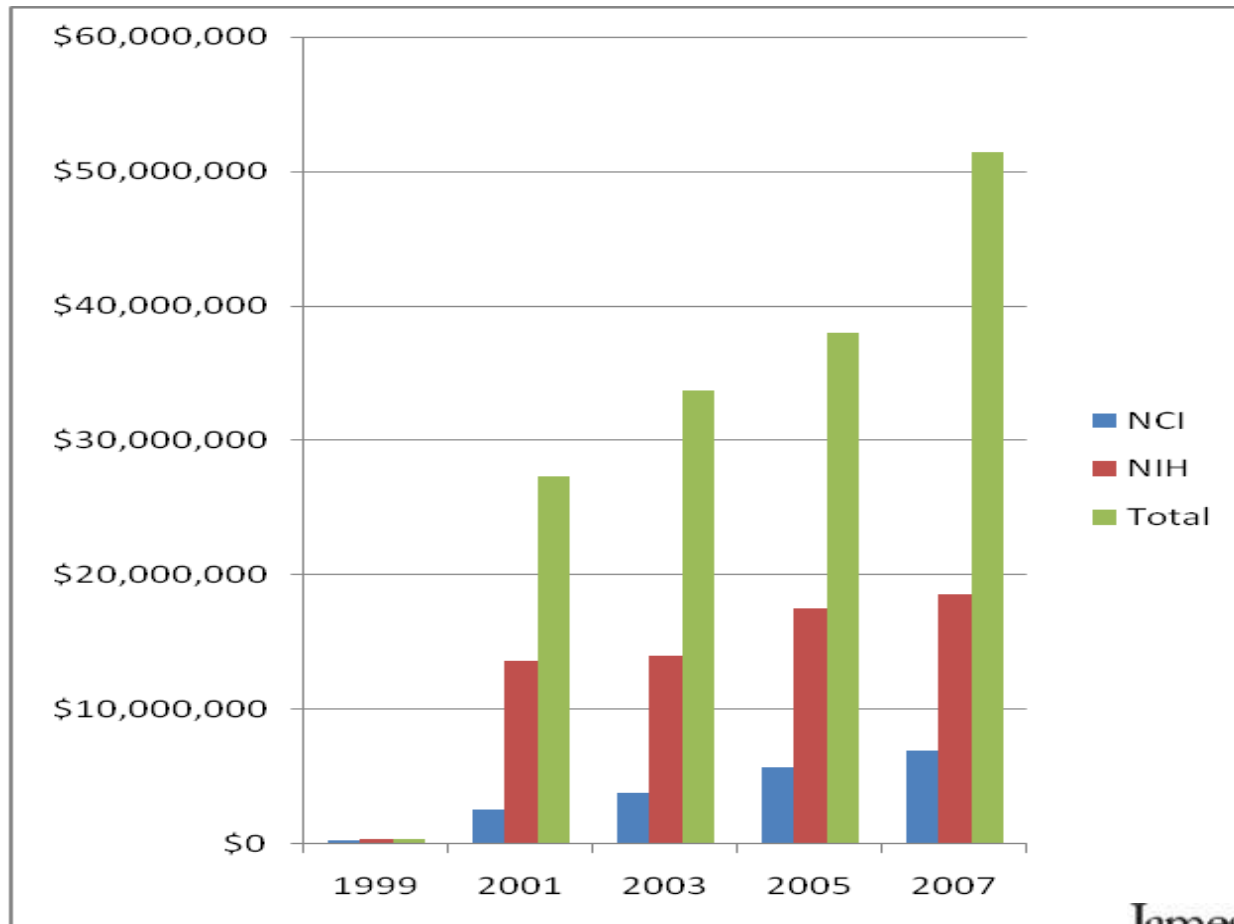
COBRE INVESTIGATOR HISTORY

<u>PI</u>	<u>Start</u>	<u>Project #</u>	<u>Funding Institute</u>
• Jason Chesney	original	1 8/19/05	NCI
• Robert Mitchell	original	2 7/01/04	NCI
• Binks Wattenberg	original	3 7/15/05	NCI
• Pawel Kozlowsky	original	4 3/31/04	euthanized
• Hong Ye	original	5 7/01/07	GM
• Chi Li	2/01/06	6	
• Clark, Geoffrey	7/01/06	7 6/30/10	NCI
• Qiutang Li	10/01/06	8 8/31/10	NEI
• Al Cunningham	4/01/07	9	
• Magda Kucia	7/01/07	10	
• Brian Clem	8/01/10	11	
• Kavitha Yaddanapudi	10/01/10	12	

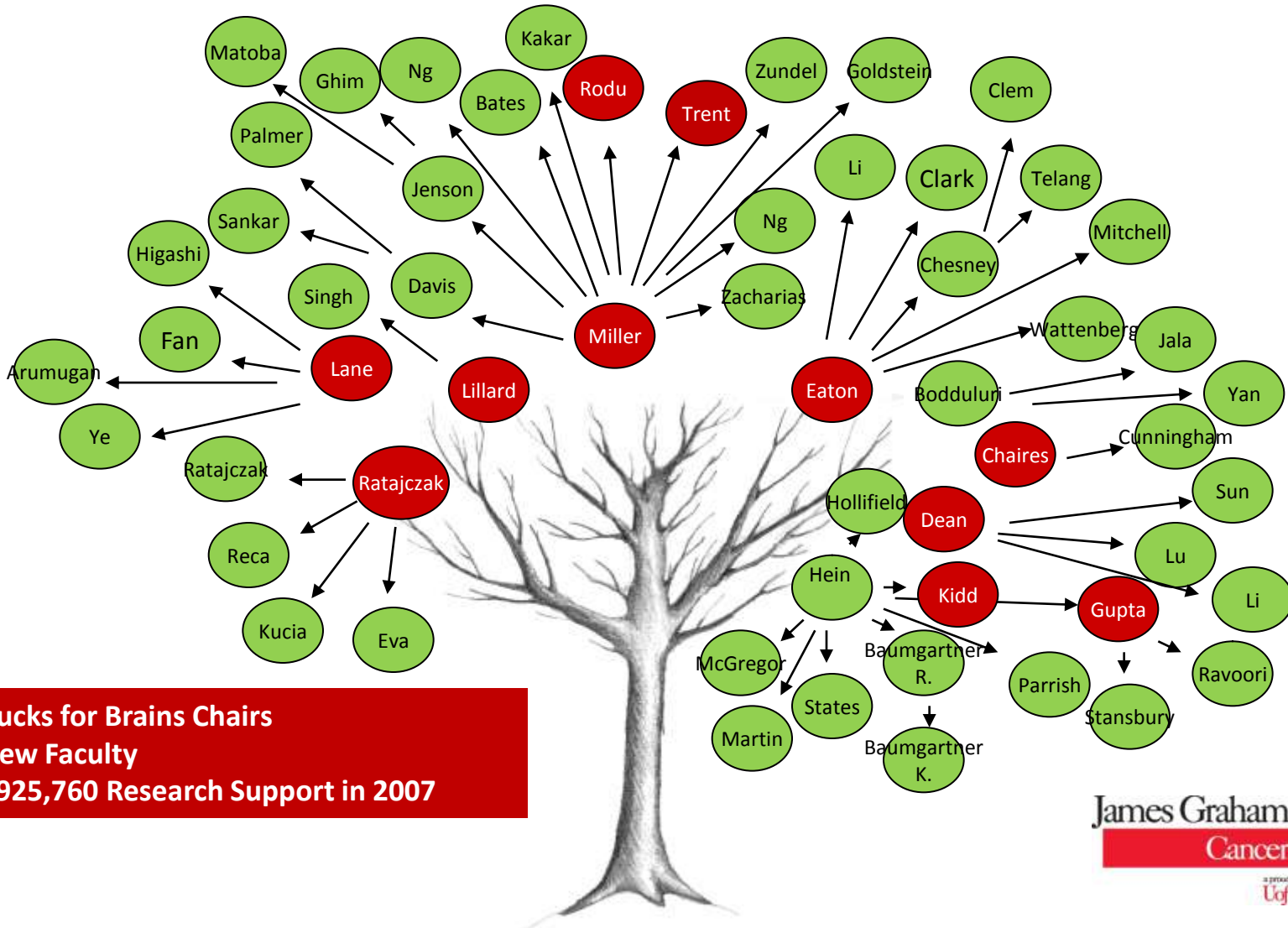
BCC Drug Development Program

- Molecular Targets Program
 - 40 scientists focused on target identification and verification
 - Major foci include cancer metabolism, quadruplex DNA and telomerase
- Structural Biology Program
 - 14 physical scientists focused on drug development and cancer cell metabolism
 - Based in Medical School and Department of Chemistry

BCC Research Support



The Role of “Bucks for Brains” at BCC

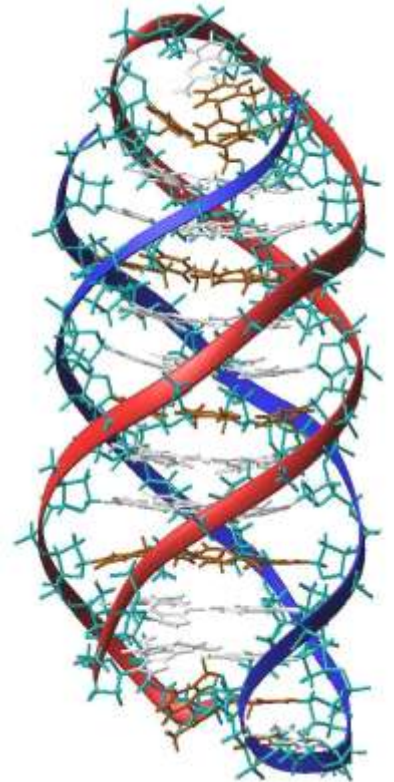


11 Bucks for Brains Chairs
58 New Faculty
\$26,925,760 Research Support in 2007

AS1411

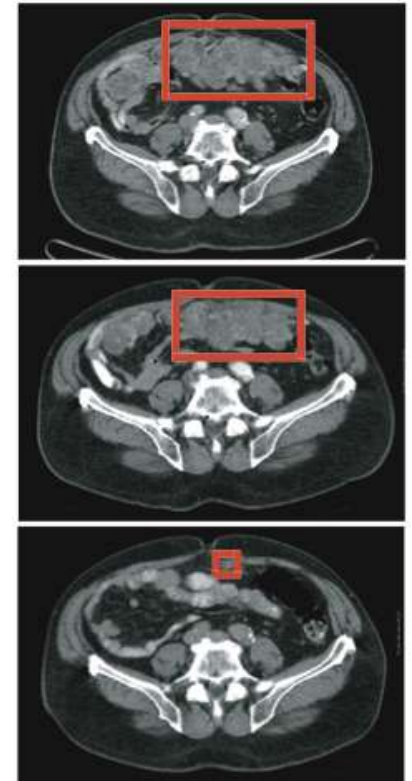
DNA Aptamer as Cancer Therapeutic

- Phase I study of AS1411 completed at BCC; Phase II underway worldwide
- More than 30 patients treated with no toxicity
- >50% responses in patients with renal cell cancer, one complete remission at four years



Development of AS1411

- AS1411 was developed at the Brown Cancer Center
- All of the preclinical development done with NIH and DOD funding
- Aptamera, Inc. founded by Drs. Bates, Trent and Miller
- Phase I clinical trial performed at Brown Cancer Center
- Now in Phase II clinical trials with Antisoma



Cervical Cancer Vaccine Gardasil

- Developed at Georgetown by Drs. Bennett Jenson and Shin-Je Ghim
- First 100% effective cancer vaccine
- Will also play a role in head and neck and lung cancers
- Costs \$360 per person to inoculate



Tobacco-Based HPV Vaccine

- Created at Brown Cancer Center/OCRCP
- Now licensed and being developed in collaboration with ACT
- Will likely be much less expensive to produce (\$0.01 to \$0.05 per dose)
- Completely effective in canine model



BCC Drug Development Pipeline

Target/Drug	“Drug”	In Vitro	Animal Data	IND	Phase I Clinical Trial	Phase II Clinical Trial
Nucleolin – AS1411	X	X	X	X	X	X
β-Glucan	X	X	X	X	X	X
Na/K ATPase	X	X	X	X	X	
Protex	X	X	X	X	X	
Microencapsulated IL-2	X	X	X	X		
HPV Vaccine	X	X	X			
IPFK2	X	X (30)	X			
MIF	X	X (25)	X			
PU27	X	X (8)	X			
CXCR4	X	X (9)				
Transaldolase	X	X				
LDH	X	X				
BLT1	X	X				
Nucleolin (small molecule)	X	X				
Stem Cell Antigens	X	X	X			
Telomerase	X	X				



Brown Cancer Center Drug Development Infrastructure

Brown Cancer Center

Shared Facilities for Drug Development

- Clinical Trial Facility
 - >30 FTE oversee 124 studies ranging from Phase I to Phase III
- Structural Biology Shared Facilities
 - NMR Core Facility
 - Xray Crystallography Shared Facility
 - Molecular Modeling Core Facility – Dataseam Grid
 - Biophysics Shared Facility
 - Protein Production and Purification Facility

Advanced Cancer Therapeutics (ACT)



- Biotech startup company owned by University of Louisville/BCC and local investors
- Novel business model which is financed by local investors and pharmaceutical partners
- Developing novel cancer therapeutics from the Brown Cancer Center through Phase I clinical trials
- Will allow the Brown Cancer Center to develop 2-3 new drugs per year
- Eight fulltime chemists in India synthesizing new drugs
- Early phase clinical trials will be done in Kentucky with Kentucky citizens as patients

Kosair Pediatric Cancer Research Program

- \$12 M gift from Kosair Foundation
- Directed by Dr. John Trent
- Will allow recruitment of 8-10 new translational scientists focused on “pediatric targets”
- Will interface with ACT for rapid drug development
- Will be part of BCC Drug Development Program

Wendell Cherry Clinical Trial Institute

- Six endowed positions (three \$2M chairs and three \$1M professorships)
- Infrastructure to perform early phase clinical trials
- Statewide clinical network
- Will allow rapid translation of BCC discoveries to early phase trials

Brown Cancer Center Translational Research:

Leveraging Support

